A Phase I Clinical Study Evaluating the Safety, Tolerability, Pharmacokinetic (PK) Characteristics, and Preliminary Efficacy of Intratumoral Injection of Ferrous Ion Adsorbed Carbon Nanoparticle Suspension Injection (CNSI-Fe) in Patients with Advanced Solid Tumors

Informed Consent Form

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Screening Number:

Investigator: Yongsheng Wang

Clinical Trial Institution: West China Hospital, Sichuan University

Trial Site Address: No. 37 Guoxue Lane, Wuhou District, Chengdu, Sichuan Province

Sponsor: Sichuan Enray Pharmaceutical Technology Company

Informed Consent Form · Information Page

Please read the following content carefully and ensure that you fully understand this consent form before signing on the last page!

[Introduction to the Informed Consent Form]

We invite you to participate in a Phase I clinical study of Ferrous Ion Adsorbed Carbon Nanoparticle Suspension Injection (CNSI-Fe) in patients with advanced solid tumors, initiated by Sichuan Enray Pharmaceutical Technology Company. Based on your current condition, you may be eligible to participate in this clinical research. We will provide you with some important information for your reference.

This study will be conducted at West China Hospital, Sichuan University. Before you decide whether to participate in this study, please read the following content carefully to help you understand the purpose of this study, the aspects it involves, as well as the potential benefits, risks, and discomforts you may experience if you decide to participate. You also have the right to voluntarily participate in or withdraw from the trial at any time. If you have any questions or need more information during the reading process, please feel free to contact the investigator, who will answer any questions you may have.

Your participation in this clinical study is entirely voluntary. The investigator will provide you with detailed information about the content of this trial and interpret this Informed Consent Form together with you. If, after careful consideration, you agree to participate in the trial, please sign the informed consent form, and you will

receive a copy of the form with the investigator's signature.

[Study Overview]

Ferrous Ion Adsorbed Carbon Nanoparticle Suspension Injection (CNSI-Fe) is an innovative anticancer drug developed by Sichuan Enray Pharmaceutical Technology Company, which is a nanosuspension formulation with iron ions as the active pharmaceutical ingredient. After the iron ions in CNSI-Fe enter cancer cells, a series of chemical reactions occur, affecting the membrane function of tumor cells, leading to cancer cell death, thereby achieving the therapeutic effect on malignant tumors.

This study, titled "Phase I clinical study to evaluate the safety, tolerability, pharmacokinetic (PK) characteristics, and preliminary efficacy of intratumoral injection of Ferrous Ion Adsorbed Carbon Nanoparticle Suspension Injection (CNSI-Fe) in patients with advanced solid tumors," is led by West China Hospital, Sichuan University, with Professor Yongsheng Wang as the principal investigator. It is the first study of CNSI-Fe in the Chinese population with solid tumors and aims to provide new and important clinical treatment options for patients with advanced solid tumors.

This study has been approved by the National Medical Products Administration and will be conducted at 3 to 6 research centers nationwide, with approximately 15 to 30 patients enrolled.

This study has been approved by the Clinical Trial Ethics Committee of West China Hospital, Sichuan University, and will be conducted at West China Hospital.

[Study Objectives]

The main objective of this study is to evaluate the safety and tolerability of intratumoral injection of Ferrous Ion Adsorbed Carbon Nanoparticle Suspension Injection (CNSI-Fe) at different doses in patients with advanced solid tumors. It aims to observe dose-limiting toxicity (DLT) of CNSI-Fe and determine the maximum tolerated dose (MTD) or the highest injectable dose in humans as a basis for dose selection in subsequent clinical studies. The secondary objectives are to evaluate the pharmacokinetic (PK) characteristics of CNSI-Fe at different doses and to preliminarily assess the efficacy of CNSI-Fe in patients with advanced solid tumors. The exploratory objectives are to evaluate the intratumoral pharmacodynamics (PD) characteristics of CNSI-Fe at different doses (not mandatory), to evaluate the intratumoral PK characteristics of CNSI-Fe in patients with advanced solid tumors (not mandatory), and to explore the dose-response relationship between tumor size and CNSI-Fe injection dose/concentration (not mandatory).

[Inclusion Criteria] You need to meet all the following criteria to be eligible for this trial:

1. Understand and voluntarily sign the written informed consent form (ICF) and be willing and able to comply with all trial requirements.

2. Be a male or female aged 18 to 80 years (inclusive) at the time of signing the ICF.

3. Have a histologically or cytologically confirmed advanced solid tumor, and the

current standard treatment is ineffective (disease progression after treatment or inability to tolerate treatment) or there is no effective standard treatment available, such as colorectal cancer, pancreatic cancer, breast cancer, stomach cancer, cervical cancer, lung cancer, head and neck cancer, bile duct cancer, kidney cancer, prostate cancer, vulvar cancer, etc.

Note: Late-stage solid tumor patients who cannot receive standard treatment for any reason, or patients with tumor types that are insensitive to existing standard treatments (such as pancreatic cancer, undifferentiated thyroid cancer, and sarcoma), and who experience disease progression after receiving standard treatment for the first time are allowed to participate.

4. According to RECIST v1.1, there must be at least one measurable lesion that has not been previously undergone radiation therapy (unless the lesion has clearly progressed after radiation therapy) and has not undergone tissue biopsy within 7 days prior to the first dose.

5. The presence of injectable lesions (able to be directly injected or assisted by medical imaging instruments).

6. ECOG performance status of 0-1 within 7 days prior to the first dose.

7. Expected survival of ≥12 weeks.

8. Adverse drug reactions (ADR) caused by previous treatments have recovered to grade 1 or below according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v5.0 standards, excluding alopecia.

9. Left ventricular ejection fraction (LVEF) ≥50%.

10. Adequate hematological and organ function within 7 days prior to the first dose, with laboratory test results meeting the following criteria:

a) Hematology:

Absolute neutrophil count (ANC) ≥1.5×10^9/L without the use of granulocyte colony-stimulating factor (G-CSF) within 14 days prior to the hematological laboratory test.

Platelet count (PLT) ≥90×10^9/L without platelet transfusion within 14 days prior to the hematological laboratory test.

Hemoglobin (Hb) ≥90 g/L without blood transfusion or use of erythropoietin within 14 days prior to the hematological laboratory test.

b) Renal function:

Serum creatinine (Cr) ≤1.5 times the upper limit of normal (ULN) or calculated creatinine clearance (Ccr) ≥ 50 mL/min using the Cockcroft-Gault formula (calculated only when baseline Cr >1.5 times ULN).

c) Liver function:

Total bilirubin (TBIL) ≤1.5 times ULN (≤3.0 times ULN for patients with Gilbert's syndrome or liver metastasis).

Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) ≤3 times ULN. Patients with confirmed liver metastasis or bone metastasis must meet the following conditions:

Patients with confirmed liver metastasis: AST and ALT ≤5 times ULN.

Patients with confirmed bone metastasis: ALP ≤5 times ULN.

Serum albumin ≥2.8 g/dL.

d) Coagulation function:

International Normalized Ratio (INR) or Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT) ≤1.5×ULN;

Note: If the injection site is in the skin and/or subcutaneous tissue and the patient is receiving anticoagulant therapy, it is allowed for INR, PT, and aPTT to be prolonged, as excessive bleeding can be controlled by applying direct pressure, as determined by the investigator.

11. Women of childbearing potential (WOCBP) must have a negative pregnancy test result within 7 days prior to the first dose of the investigational drug and must commit to using effective contraception or abstinence during the study drug treatment period and for 6 months after the end of the study drug treatment. In addition, female patients must be non-lactating and agree not to donate eggs during this period;

Note: WOCBP is defined as non-sterilized women who have experienced menarche but have not undergone sterilization procedures (hysterectomy or bilateral oophorectomy) and are not in the postmenopausal period. Postmenopausal is defined as continuous amenorrhea for ≥12 months in a woman over 45 years of age in the absence of other biological or physiological reasons. In addition, women under 55 years of age must have serum follicle-stimulating hormone (FSH) levels >40 mIU/mL to confirm postmenopausal status. Hormone replacement therapy (HRT) may artificially suppress FSH levels in women and may require a washout period to return

to physiological FSH levels. The duration of the washout period is one of the factors influenced by the type of HRT. The following washout period durations are recommended as guidelines, and the investigator should judge the results of serum FSH level testing:

□Vaginal hormone preparations: at least 1 week (ring, cream, gel);

□Transdermal preparations: at least 4 weeks;

□Oral preparations: at least 8 weeks;

□Other gastrointestinal preparations may require a washout period of up to 6 months.

If the serum FSH level is >40 mIU/mL during the washout period, the woman can be considered postmenopausal.

12. Male patients must commit to using effective contraception or abstinence during the study drug treatment period and for 6 months after the end of the study drug treatment. In addition, male patients must agree not to donate sperm.

[Exclusion Criteria] You are not eligible to participate in this trial if you meet any of the following conditions:

1. History or current presence of iron metabolism disorders (except for patients with iron deficiency anemia), such as thalassemia, favism (glucose-6-phosphate dehydrogenase deficiency), etc.

2. History or current presence of signs of cavity organ perforation at the injection site.

3. History or current presence of local skin breakdown, redness, necrosis, bleeding, or any other condition that may affect the injection of the investigational drug at the

injection site.

4. Target lesions have received radiotherapy or any other anti-tumor drug treatment within 4 weeks prior to the first administration of the investigational drug, or the time since the last anti-tumor treatment [including but not limited to chemotherapy, targeted therapy, immunotherapy, National Medical Products Administration (NMPA) approved anti-tumor traditional Chinese medicine, and Chinese herbal medicine with anti-tumor effects] has not reached 5 half-lives, whichever is shorter.

5. Major surgery or significant trauma (excluding diagnostic procedures) or unhealed wounds and ulcers within the past 4 weeks prior to the first administration of the investigational drug.

6. Presence of life-threatening clinical manifestations of brain and central nervous system metastasis at the time of enrollment.

7. Poorly controlled hypertension (systolic blood pressure ≥150 mmHg or diastolic blood pressure ≥100 mmHg).

8. Uncontrolled tumor-related pain.

9. Uncontrolled pleural effusion, pericardial effusion, or ascites requiring repeated drainage (once/month or more frequently);

10. Presence of other malignant tumors within 5 years prior to the initiation of the study treatment, except for non-melanoma skin cancer, localized prostate cancer, ductal carcinoma in situ, stage I uterine cancer, cervical carcinoma in situ, or breast carcinoma in situ that has already received curative treatment;

11. Vaccination with live virus vaccines within 4 weeks prior to the initiation of the

study treatment;

Note: Injectable seasonal influenza vaccines are usually inactivated influenza vaccines and are allowed; however, intranasal influenza vaccines (e.g., FluMist®) are live attenuated vaccines and are not allowed.

12. History of immunodeficiency, including human immunodeficiency virus (HIV) positive status or acquired/congenital immunodeficiency diseases, or history of organ transplantation;

13. Active hepatitis B virus (HBV) infection [positive for hepatitis B surface antigen (HBsAg) or hepatitis B core antibody (HBcAb) and HBV deoxyribonucleic acid (DNA) quantification >500 IU/mL], hepatitis C virus (HCV) infection [positive for HCV antibody and hepatitis C ribonucleic acid (RNA) by polymerase chain reaction (PCR) exceeding the upper limit of normal (ULN)], positive for anti-human immunodeficiency virus antibody (Anti-HIV). Any of the above criteria apply;

14. Severe chronic or active infection (including tuberculosis infection) requiring systemic antibacterial, antifungal, or antiviral therapy within 4 weeks prior to the initiation of the study treatment;

Note: Antiviral therapy is allowed for patients with viral hepatitis.

15. Severe cardiovascular disease, including but not limited to:

Acute coronary syndrome or history of coronary artery intervention/stent implantation/coronary artery bypass grafting within the past 6 months;

New York Heart Association (NYHA) class II-IV congestive heart failure (CHF), or history of NYHA class III or IV CHF.

16. Active psychiatric disorders (schizophrenia, severe depressive disorder, bipolar disorder, etc.);

17. Known allergy or intolerance to the active ingredients, excipients, or other iron supplements used in the investigational drug;

18. Participation in other interventional clinical studies within 4 weeks prior to the initiation of the study treatment (calculated from the first day after the last administration of the previous study, except for interventions with non-interventional drugs or investigational medical devices);

19. Other conditions in which the investigator deems the patient unsuitable for participation in this trial.

[Study design and steps]

This study is an open-label, multicenter, dose-escalation Phase I clinical trial. If you meet the inclusion criteria and agree to participate in this study, you will receive CNSI-Fe treatment. Based on preclinical animal study results, this study plans to start the dose-escalation phase with a dose of CNSI-Fe 30 mg, followed by escalating doses of 30 mg, 60 mg, 90 mg, and potentially adjusted to 75 mg, 120 mg, 150 mg, or even higher doses. Each dose group will consist of 3-6 patients who will receive intratumoral injection of the specified dose of CNSI-Fe on the first day. Each dose group will undergo dose-limiting toxicity assessment in at least 3 patients before proceeding to the next dose group.

The entire study procedure includes a screening period, treatment period, and

follow-up period.

The screening period lasts for a maximum of 28 days. After completing screening examinations and assessments, eligible patients will be enrolled in the treatment period. During the treatment period, patients will receive up to two doses of CNSI-Fe (with a 21-28 day interval between doses). You will need to visit according to the dosing frequency and complete relevant examinations and assessments before and after each dose. The follow-up period is for safety follow-up and will occur approximately 28 days after the last dose. If you terminate or end the treatment early, you will need to undergo a study treatment termination visit according to the study protocol, which includes completing relevant examinations and assessments. Your study doctor will also discuss precautions and future potential treatments and medications with you.

(1) Screening Period:

Before entering the screening period, you need to read this Informed Consent Form (ICF). If you fully understand the content of the ICF and voluntarily agree to participate in this study, you need to sign the ICF. After signing the ICF, you will enter the screening period, during which you will undergo the following examinations and assessments at the hospital to help your study doctor determine if you are suitable for participation in this study.

Within the first 28 days before the initial dose, the following items need to be completed:

1. Sign the Informed Consent Form.

2. Collect your basic information, including gender, age, and ethnicity/race.

3. Measure your height and weight.

4. The study doctor will ask and record your medical history and treatment history in detail, including your past medical history, medication history (within the 4 weeks before screening and ongoing concomitant treatment), past history of all tumors (including tumor staging, diagnosis date, genetic testing results), past history of all anti-tumor treatments, family history, surgical history, immunization history, allergy history, smoking history, history of drug abuse/dependence, etc. The study doctor may need you to provide relevant records from other hospitals, please cooperate in providing them.

5. Measure your respiration, pulse/heart rate, blood pressure, and body temperature.

6. Undergo a comprehensive physical examination.

7. Perform a 12-lead electrocardiogram (ECG) examination.

8. Perform a transthoracic echocardiogram examination.

9. Collect your blood samples for glucose-6-phosphate dehydrogenase testing, iron examination, myocardial enzyme spectrum testing, follicle-stimulating hormone (FSH) testing (only for postmenopausal women over 45 years old but under 55 years old), viral serology testing.

10. Collect tumor tissue samples (exploratory pharmacodynamics PD indicator testing, intratumoral pharmacokinetics PK study), not mandatory.

11. Perform tumor evaluation for the brain, chest, abdomen, pelvis, and other suspected tumor lesions.

12. You will be asked some questions about your physical condition. If you have any physical discomfort, please inform the study doctor.

Within the first 7 days before the first dose of medication, the following tasks need to be completed:

1. Assess your physical condition;

2. Collect your blood samples for complete blood count, blood biochemistry tests, coagulation function tests, pregnancy tests (for women of childbearing age only), and tumor marker tests;

3. Collect your urine sample for urinalysis;

4. Ask you some questions about your physical condition. If you experience any discomfort, please inform the research doctor.

After completing all these assessments and tests, if you are unable to meet all the inclusion criteria, you may not be able to participate in this study. You can choose alternative treatments, including other medications or symptomatic treatment. The research doctor will discuss the best treatment options with you. If you need more detailed information about the inclusion criteria or have any questions about the inclusion criteria, please feel free to ask your research doctor.

(2) Treatment Period:

During the treatment period, if you meet the criteria and agree to participate in this study, you will be assigned to a dose group (which may be 30 mg, 60 mg, 90 mg, 75 mg, 120 mg, 150 mg, or even higher doses, depending on the progress of the study) in the order of enrollment. You will enter the first cycle (dose-limiting toxicity

assessment period) and receive a specified dose of CNSI-Fe intratumoral injection on Day 1. Safety checks will be conducted on Day 7, Day 14, and Day 21 to evaluate dose-limiting toxicity. Additionally, imaging examinations will be performed in the third to fourth week to evaluate efficacy. If your study doctor determines that the benefits of continuing treatment outweigh the risks based on safety and efficacy assessments, you will enter the second cycle (maintenance treatment period) within 7 days after the end of the first cycle. During the second cycle, you will receive a second CNSI-Fe intratumoral injection at the same dose as the initial dose, and clinical examinations will be conducted as in the first cycle. If your study doctor determines that the benefits of continuing treatment are less than the risks, you will not enter the second cycle and will proceed directly to the follow-up period.

During each treatment cycle, your active cooperation in various examinations and treatments is required. Your study doctor will regularly conduct various clinical examinations according to the study protocol, including imaging examinations of the tumor, to evaluate the safety and efficacy of the study drug treatment. During your visits to the clinic, please inform the study doctor proactively about any physical discomfort you experience, including the duration and symptoms. The study doctor will also assess your physical condition through various examinations and interviews. The examinations you need to complete include:

1. Measurement of body weight (performed on Day 1 of each cycle).
2. Measurement of respiration, pulse/heart rate, blood pressure, and body temperature (performed on Day 1, Day 7, Day 14, and Day 21 of each cycle).

3. Comprehensive physical examination (performed on Day 1 of each cycle and when deemed necessary by the study doctor).

4. Assessment of your physical fitness (performed on Day 1 and Day 21 of each cycle).

5. 12-lead electrocardiogram (ECG) examination (performed within 2 hours before administration on Day 1, 0.5 hours ± 5 minutes after administration, 4 hours ± 30 minutes after administration, 8 hours ± 30 minutes after administration, 24 hours ± 30 minutes after administration, 48 hours ± 30 minutes after administration, 72 hours ± 30 minutes after administration, on Day 7, Day 14, and Day 21, and continuous ECG monitoring within 8 hours after CNSI-Fe administration; the study doctor may consider increasing the frequency of 12-lead ECG examinations during the trial for your safety).

6. Collection of blood samples for iron examination (collected within 24 hours before administration on Day 1, 5 minutes ± 1 minute after administration, 15 minutes ± 2 minutes after administration, 30 minutes ± 5 minutes after administration, 2 hours ± 30 minutes after administration, 6 hours ± 30 minutes after administration, 10 hours ± 30 minutes after administration, on Day 7, Day 14, and Day 21; the study doctor may consider increasing the frequency of testing for your safety).

7. Collection of blood samples for complete blood count and blood biochemistry examination (performed on Day 7, Day 14, and Day 21; the study doctor may consider increasing the frequency of examinations for your safety).

8. Collection of blood samples for coagulation function examination (performed on

Day 7 and Day 21 of each cycle).

9. Collection of blood samples for tumor marker detection (performed on Day 21 of each cycle).

10. Collection of urine samples for urinalysis (performed on Day 7, Day 14, and Day 21 of each cycle).

11. Echocardiography examination (performed if necessary).

12. Collection of blood samples for myocardial enzyme spectrum detection (performed if necessary).

13. Collection of blood samples for pharmacokinetic analysis (see the section on biological sample collection in the study for specific blood collection time points).

14. Collection of tumor tissue samples (exploratory PD marker detection, intratumoral PK study), not mandatory to provide.

15. Inquiring about any changes in your health during the study period and informing the study doctor of any health conditions related or unrelated to the treatment.

16. Inquiring about all other medications and treatments you have used during the study period.

17. Tumor evaluation for suspected tumor lesions in the brain, chest, abdomen, pelvis, and other areas.

(3) Followed-up period

During the follow-up period, which occurs 28 days (±3 days) after the last dose, you will need to visit the research center for a check-up and evaluation. The following examinations and assessments will be conducted, unless you have already undergone

them within the 3 days prior to the visit:

1. Measurement of respiration, pulse/heart rate, blood pressure, and body temperature.

2. Comprehensive physical examination.

3. Assessment of your physical condition.

4. 12-lead electrocardiogram (ECG) examination.

5. Collection of blood samples for complete blood count, blood biochemistry, coagulation function, pregnancy test (only for women of childbearing age), tumor marker detection, and iron examination.

6. Collection of urine samples for urinalysis.

7. Inquiry about any changes in your health condition during the study period. You need to inform the research doctor about any health-related changes, regardless of whether you think they are related to the treatment you received.

8. Inquiry about all other medications and treatments you have used during the study period.

Note:

- If your initial tumor imaging evaluation shows complete remission or partial remission, you will need to return to the research center for a repeat evaluation to confirm the efficacy at least 4 weeks later.
- Throughout the entire trial period, you will need to complete the scheduled visits and related examinations as required by the protocol.

[Duration of the Study]

If you decide to participate in this study, the maximum duration of the trial will be approximately 4 months.

If, after the study, the evaluation of tumor efficacy shows complete remission or partial remission, and your research doctor determines that continued treatment with the study drug would still be beneficial, you may continue to receive the study drug until disease progression, intolerable toxicity occurs, or the sponsor decides to terminate the study.

[Unscheduled Visits]

During the trial, to ensure your medication safety, the research doctor may require additional tests beyond the scheduled visits based on your individual circumstances. The results of these additional visits will be used to evaluate the safety of your medication.

[Collection of Biological Samples during the Study]

This study will collect your biological samples, including tumor tissue sections and blood samples. The provision of tumor tissue samples is not mandatory. The tumor tissue samples you provide will be used for efficacy evaluation and intratumoral pharmacokinetic (PK) studies (not mandatory). The blood samples you provide will be used for PK analysis. Blood samples for PK analysis will be collected at the following time points:

1. CNSI-Fe first dose: PK samples will be collected within 1 hour before CNSI-Fe administration, and at 5 minutes ± 1 minute, 10 minutes ± 2 minutes, 15 minutes ± 2 minutes, 30 minutes ± 5 minutes, 1 hour ± 10 minutes, 2 hours ± 10 minutes, 4 hours ± 15 minutes, 8 hours ± 15 minutes, 12 hours ± 30 minutes, 24 hours ± 30 minutes, 48 hours ± 1 hour, and 72 hours ± 2 hours after administration.

2. CNSI-Fe Second Administration (if applicable):

The researcher may make appropriate adjustments based on the PK results of the first administration, such as adjusting the sampling time or increasing/decreasing the sampling frequency.

PK Sampling:

- Each PK sampling point requires the collection of a 3 mL blood sample for testing.
- The collection time of PK samples may be adjusted during the study period based on the latest clinical data of the drug.

Important Notes:

1. Storage Method:

All samples will be labeled with a label that only contains the subject number (anonymous code) and does not include the name.

The identity information of the subjects corresponding to the anonymous codes will be kept as original data at the research institution.

2. Destruction Time:

All samples will be used for research purposes as described in the approved

protocol.

After the study or after the analysis and testing are completed, the samples will be destroyed according to the biological sample destruction process.

[Your Rights and Obligations]

Your participation in this study is completely voluntary. You have the right to withdraw from the study at any time without facing punishment, discrimination, retaliation, or harm to your rights, regardless of whether you provide a reason for your withdrawal. If you decide to withdraw for any reason, please inform your research doctor promptly and complete the necessary termination visits, as this will help evaluate the study results.

If during the study, the research doctor obtains important information regarding the safety and effectiveness of the experimental medication that may affect your participation in this study, you have the right to be informed, and the research doctor will promptly notify you or your guardian.

If you choose to participate in this study, we hope that you will commit to and cooperate in completing the entire research process.

[Matters You Need to Cooperate With]

If you decide to participate in this study, please pay attention to the following matters and comply with the corresponding requirements during the trial period:

- You must visit the hospital according to the follow-up schedule agreed upon by

the research doctor and yourself. Your timely follow-up is crucial because the research doctor will assess whether the treatment you are receiving is truly effective.

- The research doctor will inquire about your feelings and discuss possible adverse events. Please inform the research doctor of any discomfort you experience during the trial so that appropriate measures can be taken.
- The research doctor will inquire about the medications and treatments you are currently using. If you are taking any medications, including "prescription drugs" prescribed by other doctors, "over-the-counter drugs" purchased by yourself from a pharmacy, herbal remedies, or natural therapies, please be sure to inform your research doctor.
- If you need to seek medical attention during the study for any discomfort, and the doctor who will provide the diagnosis and treatment is not your research doctor, please inform the doctor that you are participating in this clinical trial.
- During the study period and within 6 months after the end of the study medication, you should strictly use contraception. If you or your sexual partner becomes pregnant, you must immediately inform the research doctor.
- In addition to yourself, it is recommended that at least one of your family members be aware of the clinical trial you are participating in and be able to care about your condition. They should also provide feedback on your health status during follow-up visits. Your family members should promptly notify your research doctor if you experience severe discomfort (including the need for hospitalization for treatment).

• If your address, phone number, or other contact information changes, please inform your research doctor promptly.

[Supply of Study Medication After Discontinuation]

After you stop using the study medication, regardless of your medical condition, the supply of the study medication will not continue. If your condition progresses, the research doctor will advise you on other suitable treatment options.

[Risks of participating in the study]

Using any medication can potentially cause discomfort, and this study is no exception.

(1) Risks of using CNSI-Fe

The medication CNSI-Fe is currently in clinical development, and complete safety information is still being gathered. Based on preclinical animal studies and clinical research data from similar drugs, potential adverse events may include: nausea, vomiting, diarrhea, fatigue, loss of appetite, weight loss, fever, liver function damage, blood disorders, tachycardia, abnormal blood sugar levels, abnormal blood pressure, and adverse reactions related to intratumoral injection.

Since CNSI-Fe is administered via intratumoral injection, potential adverse reactions during administration may include: bleeding, infection, tumor implantation or metastasis, skin damage, pain, and allergic reactions to anesthesia.

As CNSI-Fe is composed of a carbon nanoparticle suspension injection and

ferrous sulfate for injection, according to safety data from currently marketed iron supplements, hypersensitivity reactions may occur when supplementing with iron. Additionally, since this study is an escalating dose Phase I study of CNSI-Fe, the appropriate dosage is still being explored, and CNSI-Fe may potentially lead to iron poisoning or iron overload.

CNSI-Fe does not necessarily alleviate your condition or prolong the remission period of your disease. Therefore, during your participation in this clinical trial, your condition may remain unchanged or progress.

During the treatment and follow-up period with the investigational drug, it is necessary for you to record and promptly report any adverse events you experience. The study doctor will assess and provide appropriate treatment measures or recommendations, adjust the dosing regimen if necessary, and track the prognosis and outcomes of all adverse events.

(2) Other potential adverse effects or risks of participating in the study

As part of the informed consent process, you will have a clear understanding of all risks associated with the study procedures. Measures will be taken to minimize the impact and discomfort caused by these study procedures.

- Blood sampling: Blood sampling may cause some discomfort, bleeding, or bruising at the puncture site. Small scabs or swelling may form at the site. In rare cases, fainting or local infection may occur. If you feel uncomfortable during blood sampling, please inform the study doctor or research staff promptly.
- Electrocardiogram (ECG): The placement of ECG electrodes may require

cleaning and sometimes shaving of the area. In rare cases, local skin rash or irritation may occur. Otherwise, this examination is generally risk-free.

- CT scan: CT scan is a type of X-ray imaging that involves low-dose radiation during the scanning process. You may experience claustrophobia during the scan as you need to remain still in a confined space. The study doctor may use contrast agents, which may cause pain, swelling, or mild allergic reactions such as skin rash or itching. In rare cases, contrast agents can cause life-threatening severe allergic reactions, such as anaphylactic shock. There is a slight risk of mild infection or bleeding after needle insertion into the blood vessel. If you know that you are allergic to contrast agents, please inform your study doctor and radiologist.
- MRI scan: MRI scans are generally risk-free for most people. However, if you have certain objects or devices implanted in your body, such as a pacemaker, insulin pump, ear implants, joint replacements, permanent dentures, piercings, or shrapnel, MRI scans can be very dangerous. If you are aware of any implants or objects embedded in your body, you must inform the study doctor or research staff. You may experience claustrophobia during the scan as you need to remain still in a confined space.
- If you are pregnant or planning to become pregnant, you cannot participate in this study. The effects of the study drug on unborn fetuses and breastfeeding infants are not yet clear, and the impact on sperm or semen is unknown. You or your partner must use contraception for at least 6 months after the last dose of the study drug. If you or your partner becomes pregnant during the study or within 6 months after the last dose

of the study drug, you should inform the study doctor. The study doctor will then follow up on the pregnancy. During the follow-up period, you will need to provide information about the pregnancy.

During the use of CNSI-Fe or other study procedures, adverse reactions as mentioned above may occur, although they may vary from person to person. You may not experience any adverse reactions or may experience only some of them.

In addition to the risks mentioned above, any medication and procedure may also involve unforeseen risks. If you experience any discomfort, new changes in your condition, or any unexpected situations, whether related to the study drug or not, you should promptly notify the study doctor. The study doctor will assess and provide medical treatment accordingly.

You will need to attend regular follow-up visits at the hospital during the study, undergo the specified examinations and evaluations as outlined in the study protocol. This will take up your time and may cause inconvenience or trouble.

[Pregnancy and Contraception]

CNSI-Fe has not been extensively studied with controlled clinical trials in pregnant women. Therefore, it is important to have a thorough discussion with your study doctor about all family planning options and/or alternative plans before participating in this study.

The use of CNSI-Fe during pregnancy may cause harm to the fetus. Therefore, it is recommended that both women and male participants with reproductive potential

take effective contraceptive measures throughout the entire study period and for at least 6 months after the study ends. Women should not breastfeed during their participation in this study.

If you are a woman of childbearing age, you must avoid becoming pregnant during the entire study to prevent adverse effects on fetal development and health. Before participating in the trial, you will undergo a pregnancy test to ensure that pregnant women cannot participate. If you suspect that you are pregnant during the study, please contact your doctor immediately for further guidance.

If you are a male patient, you must agree to take adequate and effective contraceptive measures or practice abstinence, and have no plans to impregnate a female partner from the date of signing this informed consent form until 6 months after the last dose of the study drug, and avoid sperm donation.

[Potential Benefits of Participation]

By participating in this clinical study, there is a possibility that your condition may improve. However, it is also possible that the expected effects may not be achieved, or disease progression may occur. The collection of tumor tissue samples/blood and other tests may not directly benefit you, but your study doctor will closely monitor your disease status during the study. Your participation will also contribute to further research and understanding of such diseases, ultimately improving the diagnosis and treatment of these conditions. We appreciate your participation in scientific research and contribution to the advancement of medicine.

[Other Treatment Options Available to You]

Your doctor will inform you about other treatment options currently available to you. You can discuss these alternative treatments with your doctor to decide whether to participate in this study.

If you decide not to participate in this study, your doctor will still advise you on other suitable treatment options.

[Prohibited Concomitant Medications and Treatments]

During the study treatment period, you need to avoid using the following medications or treatments:

- Other anti-tumor treatments (including but not limited to chemotherapy, radiation therapy, immunotherapy, targeted therapy, approved anti-tumor Chinese medicine, surgery, etc.), including experimental treatments or approved anti-tumor treatments.
- Other concomitant medications/treatments that may affect the evaluation of the primary endpoints, as determined by the study doctor.

[Regarding Fees]

The sponsor provides the investigational drug (CNSI-Fe) free of charge. The sponsor will cover all examination costs related to the trial during the study period.

However, the costs for examinations and treatments related to other concurrent diseases and the best supportive care for your condition will not be reimbursed.

As a participant, you will not receive any compensation for participating in this study. However, you will receive some reasonable allowances, as follows:

- A transportation allowance of 200 yuan will be provided for each visit to the study center.
- A nutrition allowance of 200 yuan will be provided for each PK blood sample collection, as PK analysis requires your blood samples. The PK study for the first administration of CNSI-Fe will involve 13 PK blood collections, totaling a nutrition allowance of 2600 yuan. The PK study for the second administration of CNSI-Fe (if applicable) will provide a corresponding nutrition allowance based on the actual number of blood collections (200 yuan per collection).
- A work absence allowance of 1000 yuan will be provided for PK blood collections that need to be conducted at the hospital.
- A subsidy of 500 yuan will be provided for each tissue sample collection for efficacy evaluation and intratumoral PK study. The study anticipates a maximum of 2 tissue collections, thus providing a maximum subsidy of 1000 yuan (final subsidy will be based on the actual number of collections).

All the above allowances will be settled based on the actual number of visits.

[Handling of Damages]

If you experience any adverse events related to the trial during the study period, please inform your investigator promptly. The investigator will provide you with timely and scientific free treatment (the medical expenses will be borne by Sichuan

Enray Pharmaceutical Technology Company.). In the case of severe adverse events related to the trial, besides providing free treatment, Sichuan Enray Pharmaceutical Technology Company. will provide appropriate financial compensation. All expenses will be paid by Sichuan Enray Pharmaceutical Technology Company. The company has purchased clinical trial liability insurance for this study, and you will receive corresponding compensation from the insurance company according to the insurance contract. If there are any remaining expenses that are not covered by the insurance company, Sichuan Enray Pharmaceutical Technology Company. will be responsible for compensating them, and the sponsor will handle the claims. Medical accidents caused by improper operation by medical staff during the trial will be borne by the hospital.

[Privacy and Confidentiality Principles]

Your privacy is of utmost importance to us, and we will keep your personal and medical information confidential.

The researchers at this hospital, the ethics review committee, drug regulatory authorities, other regulatory agencies, as well as the sponsor or its representatives, may review your data to ensure the accuracy of the information and compliance with legal requirements. Your research information will be identified with a specific research code, and the specific code information will be securely stored at the hospital. The information received and processed by the sponsor does not include your name or any personal information that could identify you. Any identifying information about

you will not be disclosed when publishing the research information and data obtained from this study in scientific conferences or journals.

[Conflict of Interest]

The funding for this clinical trial is provided solely by Sichuan Enray Pharmaceutical Technology Company. The researchers participating in this trial have no financial or non-financial interests that conflict with their responsibilities to the sponsor.

[Voluntary Participation in the Study]

This clinical study will adhere to the "Good Clinical Practice for Drugs" and the "Helsinki Declaration," and has obtained approval from the Clinical Trial Ethics Committee of our institution to ensure that your rights are not violated during this trial.

Whether or not to participate in the study is entirely up to you. You have the right to refuse to participate in this study or to stop using the medication or withdraw from the study at any time without affecting your relationship with your doctor or causing any loss of medical or other benefits. If you choose to withdraw from the clinical study, your research doctor will consider your safety and ask about your use of the investigational drug, and may recommend that you undergo certain medical examinations upon withdrawal. Additionally, if you fail to comply with the relevant trial requirements during the clinical study or if your research doctor deems you

unsuitable to continue participating in the trial, in order to protect your interests, the research doctor has the right to terminate your participation in the study.

[Other Information]

During the study, if the research doctor becomes aware of any important information related to the research drug that is beyond the scope of this informed consent form and may affect your suitability to continue participating in the study, the researcher will promptly notify you. If necessary, you will also need to sign a written informed consent form regarding this matter.

[Contact Information]

If you would like to learn more about this study, please contact your researcher. If you experience any discomfort during the study, you should also inform the researcher. The principal investigator of this study is Professor Yongsheng Wang. This research protocol has been approved by the Clinical Trial Ethics Committee of West China Hospital, Sichuan University. If you have any questions related to your own rights and interests, please contact the National Drug Clinical Trial Institution/GCP Center of our institution at 028-85422707; Clinical Trial Ethics Committee at 028-85423237.

In the above content, we have introduced to you the purpose, methods, potential therapeutic benefits, and possible adverse reactions of this study. If you are willing to participate in this study and can comply with the requirements of the trial protocol and

fully cooperate with the researchers, please sign this informed consent form.

This informed consent form is in duplicate, with one copy for you and one for the researcher. Please keep this document properly.

Acknowledgment: The development and progress of medical science are inseparable from clinical trials. Your participation will contribute to the advancement of medical science. We will always remember your dedication and express our sincere gratitude to you!

Informed Consent Form Signature Page

I have carefully read the information about this study and had the opportunity to discuss it with the doctor and ask questions. All my questions have been answered in a clear and understandable manner. After fully understanding the content of the informed consent form and considering the benefits and risks of participating in this study, **I voluntarily agree to participate. I understand the following:**

1. As a participant, I will comply with the requirements of the informed consent form and voluntarily participate in this study. My decision is not influenced by any individual or organization, and I have the right to withdraw from the study at any time without discrimination or retaliation. My medical treatment and rights will not be affected by my decision.

2. The results of this clinical study will only be used for research purposes. Personal information collected during the study will be kept confidential and protected according to legal regulations. The use of research results will be limited to authorized government purposes.

3. If I decide to withdraw from the study, especially due to the use of study medication, I will inform the researcher about my health condition and complete the necessary exit visit examinations. This will be beneficial for both myself and the entire study.

4. In the event of any adverse events related to the study medication, I will receive appropriate and free treatment from the researcher and the sponsor. The sponsor and/or insurance company will be responsible for any related expenses.

5. I will receive a signed copy of the informed consent form.

Participant's Name (Please print):

Participant's Signature:

Contact Phone Number:

Date and Time of Signature:

(If the participant lacks the ability to sign or understand, add or replace the following section)

Guardian's Name (Please print):

Guardian's Signature:

Relationship to Participant:

Contact Phone Number:

Date and Time of Signature:

Witness's Name* (Please print) (if applicable):

Witness's Signature:

Contact Phone Number:

Date and Time of Signature:

*The witness is an impartial individual who is not involved in the clinical trial and is not influenced by any clinical trial personnel. When the participant or their guardian lacks the ability to read, the witness reads the informed consent form and other written materials and witnesses the consent process.

Researcher's Declaration:

I confirm that I have explained the details of this trial to the participant, including their rights and the potential risks and benefits, and have provided satisfactory answers to any questions raised by the participant. The participant has expressed understanding and satisfaction.

Researcher's Name (Please print):

Researcher's Signature:

Contact Phone Number:

Date and Time of Signature: